

Exercise Interventions in Breast Cancer Survivors

Melinda L. Irwin, PhD, MPH

Assistant Professor

Department of Epidemiology and Public Health

Yale School of Medicine

Rationale for Studying Physical Activity and Breast Cancer Prognosis

- Women who are *overweight* at breast cancer diagnosis are at a 2-fold greater risk for recurrence and death compared with lighter women.
- Women who *gain weight* (~5 lbs) are at 60% increased risk of death compared women who do not gain weight.
- Obesity and weight gain leads to increased production of estrogens and insulin, which in turn, increases cell proliferation.

Rationale for Studying Physical Activity and Breast Cancer Prognosis

- Women with insulin levels in the uppermost quartile compared to women in the lowermost quartile had a
 - Two-fold increased risk of recurrence (95% CI, 1.2 to 3.3)
 - Three-fold increased risk of death (95% CI, 1.7 to 5.7)
- Physical activity has been shown to have acute and chronic effects on insulin levels in healthy women.

Rationale for Studying Physical Activity and Breast Cancer Prognosis

- High concentrations of estrogen are associated with a 2.5-fold increased incidence of postmenopausal breast cancer.
- Serum levels of estrogen were two times higher in patients who had a breast cancer recurrence than those who did not have a recurrence.
- Anti-estrogens, e.g. tamoxifen and aromatase-inhibitors, improve survival.

Proposed Biologic Mechanisms

- **Physical activity may decrease breast cancer risk or improve prognosis by:**
 - ↓ **estrogens by**
 - delaying onset of menses
 - ↓ # of ovulatory cycles
 - ↓ body fat and fat-produced estrogens
 - ↓ **insulin and IGF levels**
 - growth factors for breast epithelium for cell proliferation.

Rationale for Studying Physical Activity and Breast Cancer Prognosis

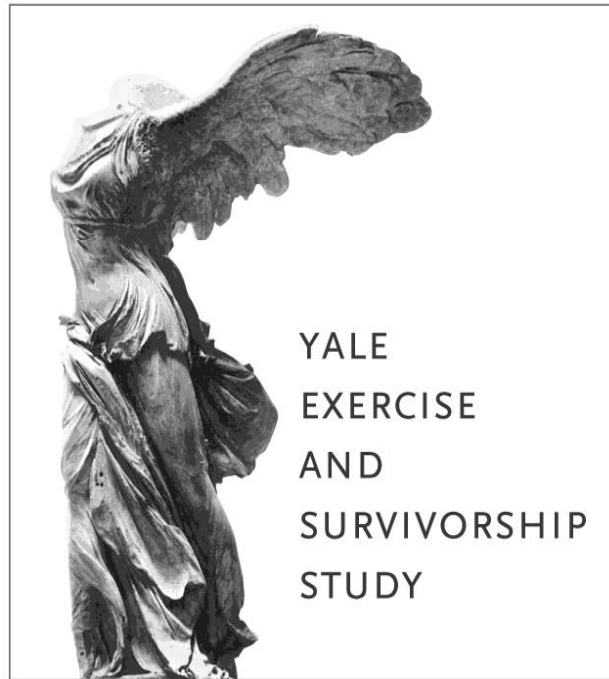
- Cancer and its treatments often produce significant morbidities that undermine quality of life.
- Exercise enhances QOL both during and after cancer treatments.

Rationale for Studying Physical Activity and Cancer Prognosis

- Physical activity associated with decreased risk of recurrence and poor survival.
 - Nurses Health Study Observational Study
 - 40% decreased risk of breast cancer death ($p = .004$) with 4-5 hr/week of brisk walking
 - Association observed only in women with ER+ and PR+ receptors

Exercise Interventions in Cancer Survivors

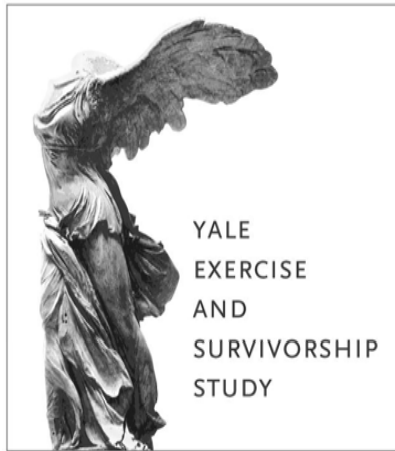
- Approximately 15 exercise interventions in breast cancer survivors; however, few studies are methodologically sound.
- Most studies focus on psychosocial rather than biological and morphological
 - Small sample sizes; short study duration, few RCTs of limited quality
 - PA is safe, feasible, improvements in fitness, QOL, nausea, fatigue, pain, and body composition.
- Few long-term cohort or intervention studies examining role of physical activity on cancer prognosis
 - Biological Markers Recurrence Survival



A Yale School of Medicine and Yale Cancer Center Research Study

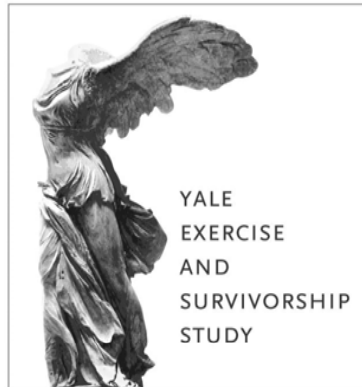
Funded by
Susan G. Komen Breast Cancer Foundation
The American Cancer Society

Melinda L. Irwin, PhD, MPH, Principal Investigator



Study Goals

- To examine the effects of a yearlong exercise program on biological mechanisms associated with breast cancer recurrence and survival.
 - Mammographic breast density
 - Fasting blood levels of insulin
 - Hormone levels (estrogens and insulin-like growth factors)
 - Body fat
 - Quality of life



Study Design

Recruit Postmenopausal Breast Cancer Survivors

Age 40 - 75 years



Check Eligibility (telephone)



Baseline Visit



GCRC Clinic Visit

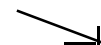


Randomize

(n = 75)



Exercise (n = 38)



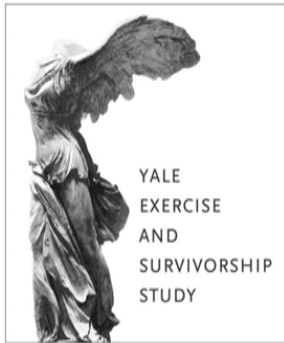
Usual Care (n = 37)



Follow-up Assessments

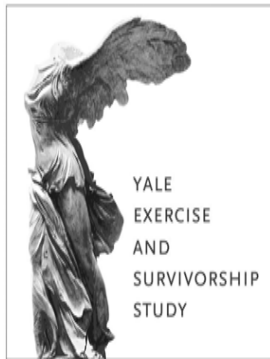
(6- and 12-months)





Eligibility Criteria

- Physician's consent to approach patient and to exercise
- Age 40 – 75
- Postmenopausal
- Currently not exercising
- Diagnosed with breast cancer 1 – 10 years ago
- Stage 0 - IIIA
- Have not had a recurrence of breast cancer or diagnosis of any other cancer
- Completed chemotherapy and/or radiation at least 6 months ago
- No major co-morbidities that limits physical activity
- Not planning to enter a structured weight loss program

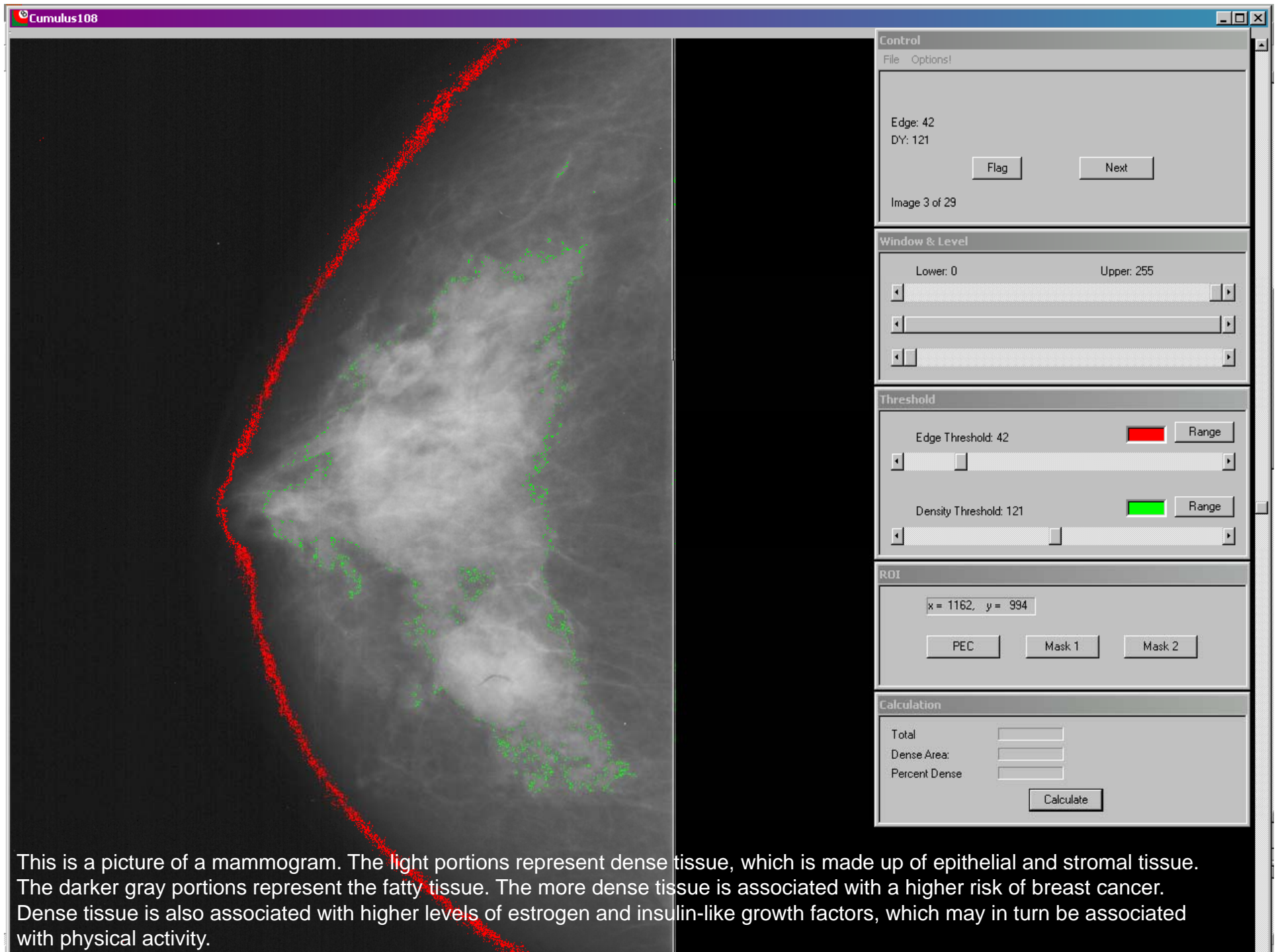


Baseline Visit

- Questionnaires
 - medical history, physical activity, etc.
- Instructions on wearing a pedometer and recording exercise for the next week
- Retrieve mammogram

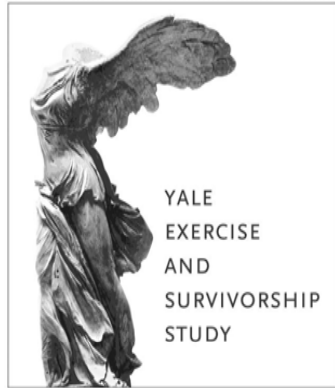
Clinic Visit

- Yale's General Clinical Research Center (located at Yale-New Haven Hospital)
- Collect pedometer and exercise log
- Fasting blood draw
- Height, weight, waist and hip circumferences
- DEXA bone density scan





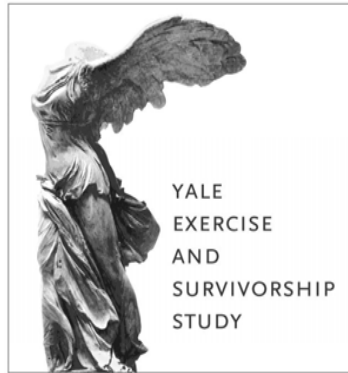




Study Groups

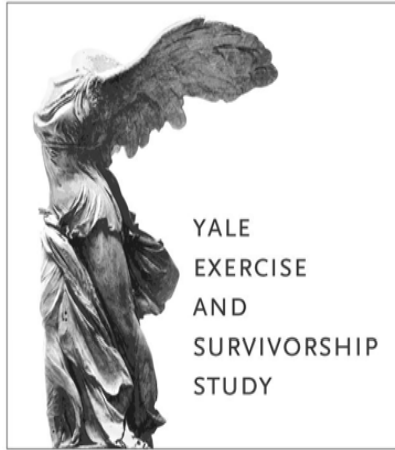
- Aerobic Exercise Group
 - 5 times/week for 1 year
 - 3 times/week supervised at health club in New Haven
 - 2 times/week unsupervised
 - » Exercise at home or at health club
 - Individualized exercise program
 - Work personally with exercise physiologist
 - Moderate-to-vigorous exercise: brisk walking, bicycling, etc.
 - Do not start a diet program.





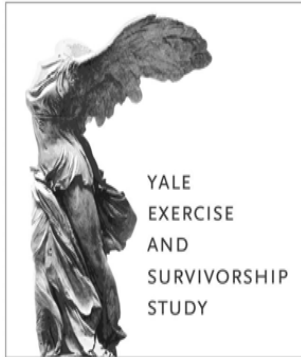
Study Groups

- Usual Care Group
 - Agree to maintain current level of physical activity for 12 months
 - At completion of study, offered three one-on-one sessions with Exercise Trainer and personalized exercise prescription
 - Do not start a diet program.



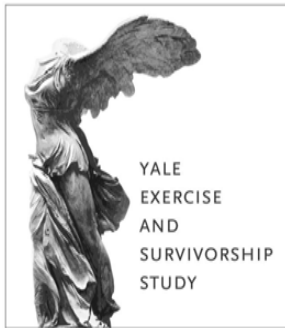
Follow Up Visits

- 6 and 12 months
 - Blood draw
 - DEXA scan (bone density/body fat)
 - Anthropometrics (height, weight, and hip/waist circumference)
 - Questionnaires
 - Pedometer and Exercise Log
 - At 12 months, mammogram retrieved from mammography facility
- Upon study completion, we will compare hormone and breast density levels between baseline, 6 and 12 months and between the two groups



Participants and Adherence

- As of October 2006
 - All 75 women have been randomized into the study and completed the study!
- Average age, education, race, stage and time since diagnosis
 - 55 yrs old
 - 54% college degree
 - 85% non-Hispanic White
 - 63% are Stage I
 - 33 months since diagnosis
- Women are exercising, on average, 132 min per week



Change in body fat and insulin

Variable	N	Baseline	Baseline to 6 months
Body fat (%)			
exercisers	29	42% \pm 5%	-0.7% \pm 1.7%*
<120 min/wk	10		-0.1% \pm 1.9%
\geq 120 min/wk	19		-1.4% \pm 1.4%*
Controls	28	40% \pm 6%	0.6% \pm 1.2%
Net difference			1.3 or ~3.2%
Insulin (pmol/L)			
exercisers	29	28.0 \pm 33.2	-1.6 \pm 13.4
<120 min/wk	10		0.1 \pm 7.2
\geq 120 min/wk	19		-2.9 \pm 16.6
controls	28	23.6 \pm 16.5	2.8 \pm 7.8
Net difference			4.4 or ~17%

Participant Quotes

- “Thank you so much for your help, support, and for turning a slug like me into an exerciser for life! And more importantly, thank you for contributing overall to breast health for women.”

Ruth Ann – Exercise Group

- “I sincerely thank you for allowing me to be a part of the research program. This program was beneficial for me both mentally and physically.”

Audrey – Exercise Group

- “The program this year has been transformative for me, and I am so grateful for having the opportunity to participate. With the program’s support, I have made regular exercise a part of my life and I feel so much better. Thank you for helping to make that possible.”

Alice – Exercise Group



Increasing or Maintaining Physical Activity during Cancer Treatment

A Yale School of Medicine and Yale Cancer Center Research Study

Funded by

The Lance Armstrong Foundation

Conclusions

- Adjuvant treatments for breast cancer lowers disease mortality 25-40%.
- Physical activity after breast cancer diagnosis may lower disease mortality ~40%.
- Results from these studies will provide important data on how much exercise is necessary to improve prognosis.
- These studies will also generate preliminary data to study the effect of exercise on breast cancer recurrence and survival.
- Advising physical activity after a cancer diagnosis may help patients as much as standard treatments.



Yale Research Team

- **Melinda Irwin**
- **Herbert Yu**
- **Beth Jones**
- **Susan Mayne**
- **Loretta DiPietro**
- **Gina Chung**
- **Marty Alvarez-Reeves**
- **Lisa Cadmus**
- **Julie Karp**
- **Rebecca Latka**
- **Andrew Wiley**
- **Eileen Mierzejewski**
- **Christian Stoddard**
- **Linda Saucier**

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